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<u>L19</u>	L18 same 15	577382	<u>L19</u>
<u>L18</u>	l5 or heating or temperature	3801972	<u>L18</u>
<u>L17</u>	l15 same l9	12	<u>L17</u>
<u>L16</u>	L15 same l3	1	<u>L16</u>
<u>L15</u>	l4 with l12	48	<u>L15</u>
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<u>L13</u>	L12 with l5	751	<u>L13</u>
<u>L12</u>	phase separation	36126	<u>L12</u>
<u>L11</u>	L10 same l8	24	<u>L11</u>
<u>L10</u>	l3 or l9	1587059	<u>L10</u>
<u>L9</u>	polymer	1553085	<u>L9</u>
<u>L8</u>	l5 same l4	40	<u>L8</u>
<u>L7</u>	L6 with l5 with l4	1	<u>L7</u>
<u>L6</u>	form? or forming	4710408	<u>L6</u>
<u>L5</u>	evaporation	311964	<u>L5</u>
<u>L4</u>	dispersed phase with continuous phase	3078	<u>L4</u>
<u>L3</u>	microparticle or microcapsule or microsphere or nanoparticle	74953	<u>L3</u>
<u>L2</u>	5789213.pn.	2	<u>L2</u>
<u>L1</u>	5849884.pn.	2	<u>L1</u>

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L21: Entry 38 of 99

File: USPT

May 1, 2001

DOCUMENT-IDENTIFIER: US 6224794 B1

** See image for Certificate of Correction **

TITLE: Methods for microsphere production

Detailed Description Text (34):

The modified solvent evaporation method that may be practiced according to the invention using, for example, the apparatus of FIG. 5, forms microspheres by the evaporation of organic solvent, thereby causing deposition of the polymer dissolved in it. The first composition, once introduced at the bottom of the column holding second composition, forms a droplet. Because the second composition is held at a temperature near or above the boiling point of the solvent present in the first composition, the droplet almost immediately becomes surrounded by a layer of solvent vapor.

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<u>L18</u>	l5 or heating or temperature	3801972	<u>L18</u>
<u>L17</u>	l15 same l9	12	<u>L17</u>
<u>L16</u>	L15 same l3	1	<u>L16</u>
<u>L15</u>	l4 with l12	48	<u>L15</u>
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<u>L9</u>	polymer	1553085	<u>L9</u>
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L21: Entry 16 of 99

File: PGPB

Nov 22, 2001

DOCUMENT-IDENTIFIER: US 20010042932 A1

TITLE: Process for preparing microparticles through phase inversion phenomena

Summary of Invention Paragraph (7):

[0007] In solvent evaporation microencapsulation, the polymer is typically dissolved in a water immiscible organic solvent and the material to be encapsulated is added to the polymer solution as a suspension or solution in organic solvent. An emulsion is formed by adding this suspension or solution to a beaker of vigorously stirring water (often containing a surface active agent to stabilize the emulsion). The organic solvent is evaporated while continuing to stir. Evaporation results in precipitation of the polymer, forming solid microcapsules containing core material.

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L1: Entry 2 of 2

File: DWPI

Dec 15, 1998

DERWENT-ACC-NO: 1999-069810
 DERWENT-WEEK: 200170
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TITLE: Microparticles for the delivery of therapeutic agents - comprise macromolecules, such as albumin, and polymers, such as hetastarch, and optionally luteinising hormone releasing hormone

INVENTOR: BLIZZARD, C D; BROWN, L R ; DI, J ; SCOTT, T L ; SUDHALTER, J ;
 WOISZWILLO, J E

PATENT-ASSIGNEE:

ASSIGNEE

EPIC THERAPEUTICS INC

CODE

EPICN

PRIORITY-DATA: 1996US-0699586 (August 19, 1996), 1993US-0028237 (March 9, 1993),
 1994US-0206456 (March 4, 1994)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5849884 A	December 15, 1998		020	C07K017/02

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
US 5849884A	March 9, 1993	1993US-0028237	CIP of
US 5849884A	March 4, 1994	1994US-0206456	CIP of
US 5849884A	August 19, 1996	1996US-0699586	
US 5849884A		US 5578709	CIP of

INT-CL (IPC): C07 K 1/00; C07 K 17/02; C08 H 1/02; G01 N 33/544

RELATED-ACC-NO: 1994-303199;1996-087113 ;1996-333665 ;1997-020467 ;2000-037296
 ;2000-564407 ;2001-606355

ABSTRACTED-PUB-NO: US 5849884A

BASIC-ABSTRACT:

Microparticle comprises a macromolecule (I) and a polymer (II) in an aqueous solution. The concentration of (I) is at least 40 %, and < 100 %, and the microparticle does not contain any oil. Also claimed is the preparation of the microparticles comprising combining (I) and (II) in an aqueous solution at a pH near the isoelectric point of (I) and exposing the solution to an energy source to form microparticles.

USE - The microparticles are used for the delivery of therapeutic agents, preferably by inhalation or injection (claimed). The microparticles are useful for a wide variety of separations, diagnostic, therapeutic, industrial, commercial, cosmetic and research applications, or for any purpose requiring the incorporation and stabilisation of an active molecule, reactant or drug. The microparticles are especially useful in medical and diagnostic applications, such as drug delivery, vaccination, gene therapy and histopathological or in vivo tissue or tumour imaging.

ADVANTAGE - The microparticles are simple, inexpensive and rapid to prepare. Their preparation permits manipulation of the microparticle release kinetics, and produces microparticles of a uniform size.

CHOSEN-DRAWING: Dwg.0/9

TI TLE-TERMS: MICROPARTICLES DELIVER THERAPEUTIC AGENT COMPRISE MACROMOLECULAR ALBUMIN POLYMER OPTION LUTEINISING HORMONE RELEASE HORMONE

DERWENT-CLASS: A96 B04 S03

CPI-CODES: A12-V01; B04-C02; B04-C03; B04-D01; B04-E03; B04-F11; B04-J05H; B04-N02; B04-N04; B12-K04; B12-K04A1; B12-M11E; B14-S03; B14-S11;

EPI-CODES: S03-E14H4;

CHEMICAL-CODES:

Chemical Indexing M1 *01*

Fragmentation Code

M423 M431 M720 M782 M903 N103 P631 P633 P831 R033

V722 V735 V741 V742 V743

Chemical Indexing M1 *02*

Fragmentation Code

M423 M431 M720 M782 M903 N103 P631 P633 P831 R033

V500 V560 V735 V741 V751 V752 V753

Chemical Indexing M1 *03*

Fragmentation Code

K0 K4 K421 M423 M431 M720 M782 M903 M904 N103

P631 P633 P831 R033 V721

Specific Compounds

10551M

Chemical Indexing M1 *04*

Fragmentation Code

D011 D601 F012 F014 F015 F423 F522 G013 G100 H1

H100 H181 H4 H401 H441 H481 H8 J0 J011 J1

J111 J171 J3 J311 J5 J521 K0 L2 L250 L9

L941 M210 M212 M273 M280 M281 M312 M313 M314 M320

M321 M332 M333 M340 M342 M343 M349 M371 M381 M391

M423 M431 M510 M511 M520 M521 M530 M531 M540 M620

M720 M782 M903 M904 N103 P631 P633 P831 R033 V901

V902 V912 V921

Specific Compounds

11749M

ENHANCED-POLYMER-INDEXING:

Polymer Index [1.1] 018 ; R24039 G3714 P0599 D01 F70 ; S9999 S1616 S1605 ; S9999 S1456*R
Polymer Index [1.2] 018 ; G3623*R P0599 D01 ; S9999 S1616 S1605 ; S9999 S1456*R Polymer Index
[1.3] 018 ; G0022*R D01 D51 D53 D12 D10 D58 ; H0000 ; H0011*R ; S9999 S1616 S1605 ; S9999
S1456*R Polymer Index [1.4] 018 ; G0271*R G0260 G0022 D01 D12 D10 D26 D51 D53 F36 F35 ;
H0000 ; H0011*R ; S9999 S1616 S1605 ; S9999 S1456*R ; P0088 Polymer Index [1.5] 018 ; G2062*R
D01 D60 F07 F35 ; H0000 ; H0011*R ; P0635*R F70 D01 ; S9999 S1616 S1605 ; S9999 S1456*R
Polymer Index [1.6] 018 ; P0964*R F34 D01 ; S9999 S1616 S1605 ; S9999 S1456*R Polymer Index
[1.7] 018 ; P1081*R F72 D01 ; S9999 S1616 S1605 ; S9999 S1456*R Polymer Index [1.8] 018 ;
P0839*R F41 D01 D63 ; S9999 S1616 S1605 ; S9999 S1456*R Polymer Index [1.9] 018 ; R03233 D01
D11 D10 D23 D22 D31 D42 D50 D76 D88 F24 F28 F26 F34 F70 H0293 P0599 G3623 ; R01863*R
D01 D11 D10 D23 D22 D31 D42 D50 D76 D86 F24 F29 F26 F34 H0293 P0599 G3623 ; S9999 S1616
S1605 ; S9999 S1456*R Polymer Index [1.10] 018 ; D63 F60 ; R01857 R01863 D01 D11 D10 D23 D22

D31 D42 D50 D76 D86 F24 F29 F26 F34 H0293 P0599 G3623 ; S9999 S1616 S1605 ; S9999 S1456*R
Polymer Index [1.11] 018 ; R00351 G1558 D01 D23 D22 D31 D42 D50 D73 D82 F47 ; P8004 P0975
P0964 D01 D10 D11 D50 D82 F34 ; P0055 ; H0000 ; S9999 S1616 S1605 ; S9999 S1456*R Polymer
Index [1.12] 018 ; G0635 G0022 D01 D12 D10 D23 D22 D31 D41 D51 D53 D58 D75 D86 F71 ;
H0000 ; S9999 S1616 S1605 ; S9999 S1456*R Polymer Index [1.13] 018 ; ND01 ; Q9999 Q7998
Q7987 ; Q9999 Q8037 Q7987 ; K9416 ; B9999 B3521*R B3510 B3372 ; N9999 N6177*R ; K9461 ;
N9999 N6439 ; N9999 N6677 N6655 ; B9999 B5209 B5185 B4740 Polymer Index [1.14] 018 ; R01740
G2335 D00 F20 H* O* 6A ; A999 A475

SECONDARY-ACC-NO:

CPI Secondary Accession Numbers: C1999-020526

Non-CPI Secondary Accession Numbers: N1999-051135



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L14: Entry 132 of 168

File: USPT

Feb 17, 1998

DOCUMENT-IDENTIFIER: US 5718921 A

TITLE: Microspheres comprising polymer and drug dispersed there within

Brief Summary Text (5):

An alternative method is the solvent evaporation or phase separation technique. The preparation of microspheres by evaporation of organic solvent from an emulsion has been disclosed by, for example, U.S. Pat. No. 3,523,906 to M. N. Vrancken and U.S. Pat. No. 3,960,757 to M. Morishita. These processes have been used extensively to prepare microspheres from biodegradable polymers, as reported in the literature and by H. Jaffe in U.S. Pat. No. 4,272,398. The procedure consists of dissolving the polymer in methylene chloride or another volatile solvent, dissolving or suspending the drug in the polymer solution and emulsifying the resulting mixture in an aqueous phase containing an emulsifier. The solvent is allowed to evaporate. The result is drug-loaded microspheres. In another variation of this method described by L. M. Sanders in J. Pharm. Science 73(9), 1294-1297 (Sept. 1984) polylactic acid microspheres are formed by suspension of the polymer in an aqueous solution. The primary disadvantage of this method with respect to polyanhydrides is the use of aqueous solutions which initiates polymer hydrolysis.

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<u>L4</u>	L3 with l2 with l1	6	<u>L4</u>
<u>L3</u>	evaporat\$	548005	<u>L3</u>
<u>L2</u>	microparticle or polymer	1560883	<u>L2</u>
<u>L1</u>	continuous with dispersed phase	3749	<u>L1</u>

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L4: Entry 1 of 6

File: PGPB

May 2, 2002

DOCUMENT-IDENTIFIER: US 20020051808 A1

TITLE: Drug delivery system involving interaction between protein or polypeptide and hydrophobic biodegradable polymer

Detail Description Paragraph (29):

[0060] Solvents for the dispersed phase and the continuous phase will of course differ in order to attain phase separation and are, therefore, selected based upon the solvent requirements for each phase. More particularly, the solvent for the dispersed phase should preferably dissolve the polymer and the incorporated agent and remain in the emulsified droplets with the drug and polymer in the continuous phase until leached out by a diluent solvent or removed by vaporization or evaporation. In this way pores are optionally formed in the drug-polymer matrix. In the case of polyglycolic acid into which water soluble markers or agents are incorporated, hexafluoroacetone sesquihydrate is an appropriate solvent. Other solvents which can be used, depending upon the characteristics of the polymer and incorporated agents, include water, hexafluoro-isopropanol, methylene chloride, acetonitrile, tetrahydrofuran, hexane and benzene. Solvents for the continuous phase should not dissolve the polymer and should emulsify the dispersed phase. Suitable solvents include, but are not limited to, benzene, dioxane, acetone, methylene chloride, chloroform, carbon tetrachloride, toluene, ethyl alcohol, acetonitrile, p-xylene, tetrahydrofuran, mineral oil, glycerin and mixtures of these solvents.

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L4: Entry 4 of 6

File: USPT

Jul 13, 1999

DOCUMENT-IDENTIFIER: US 5922357 A

TITLE: Polymer microspheres and a method of production thereof

Brief Summary Text (6):

There are various known methods for the preparation of polymeric microspheres and some of these include manipulation of the surface of the final product for a particular purpose. For example, they may be prepared directly by co-polymerisation of suitably functionalized monomers as described by Arshady in Biomaterials 14 No 1, 1993, 5-15. It is also known from U.S. Pat. No. 4,785,030 and U.S. Pat. No. 4,734,445 to produce microspheres with a hydrophilic surface using amphiphilic di-block polymers comprising a hydrophobic tail for chemical attachment to a non-water soluble core polymer. Alternatively microspheres may be generated by dissolving a suitable polymer in a solvent, dispersing the polymer solution so formed in a second liquid immiscible with the polymer solvent so as to form a dispersed phase and a continuous phase and then evaporating and/or extracting the solvent from the dispersed phase to form the polymer microspheres. In this latter method it is known, in order to prevent the droplets from coalescing or to control the droplet size, to add a surfactant material as a stabilizer to the continuous phase. This method of microsphere production is described by Arshady in Journal of Controlled Release 17 1991, 1-22, where polyvinylalcohol, polyvinylpyrrolidone, polyoxyethylene derivatives of sorbitan fatty esters and polyoxyethylene fatty ethers are mentioned as suitable surfactant stabilizers. A similar method of microsphere production is also described in EP-A-0263490 where a high molecular weight compound of sugar origin is used to stabilize the polymer droplets in the dispersion and to control the final microsphere size.